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Chief Curator: Awais Aftab

Assistant Curator: Erin Fulchiero

Curators:

Erum Ahmad
Samantha Latorre
Cheryl Chen
Christine LaGrotta
John DeMott
Rob Siedler
Prakash Mishra

Research Watch is an initiative by the residents of University Hospitals Cleveland Medical Center/ Case Western Reserve University; it aims to inform psychiatry residents and faculty of notable articles published in prominent research journals.

Journals covered in the issue:

- * American Journal of Psychiatry (AJP)
- * JAMA Psychiatry (JAMA-P)
- * The Journal of Clinical Psychiatry (JCP)
- * Lancet Psychiatry (LP)
- * Journal of the American Academy of Child & Adolescent Psychiatry (JAACAP)
- * Journal of the American Psychoanalytic Association

Contact:

muhammad.aftab@uhhospitals.org

Highlights

- Internet gaming disorder was found to have little behavioral or clinical impact on individuals in a large international survey study. (AJP)
- In a double-blind study of bipolar II depression, rates of mood switch, and treatment response rates did not differ between lithium, sertraline and combination treatment. (AJP)
- Study casts doubt on the notion that lower hippocampal volumes in late-life depression are due to prodromal Alzheimer's disease. (AJP)
- A neuropathologic study suggests that delirium and the pathologic processes of classic dementia interact to give an accelerated trajectory of cognitive decline. (JAMA-P)
- Antipsychotic drugs appear to be associated with a 1.66-fold increased risk of acute respiratory failure in patients with COPD. (JAMA-P)
- Glucose homeostasis appears to be impaired even in antipsychotic-naive first-episode schizophrenia patients, casting doubt that it is the result of chronic illness and treatment effects alone. (JAMA-P)
- While recovery rate at 9-year and 22-year follow-ups appears to be stable for bulimia nervosa, the recovery rate nearly doubles for anorexia nervosa at 22 years compared to 9 years. (JAMA-P)
- Risk of sudden death, sudden cardiac death, or total mortality for high-dose citalopram and escitalopram does not appear to differ significantly from that for other SSRIs. (JCP)
- Lurasidone adjunctive therapy significantly improved cognition in euthymic patients with bipolar I disorder with cognitive impairment in RCT. (LP)
- RCT shows that financial incentives can be effective for improving adherence to maintenance antipsychotic depot treatment in patients with psychotic disorders. (LP)
- Meta-analysis shows comparable efficacy among second-generation antipsychotics with exception for ziprasidone (inferior efficacy) and asenapine (unclear) in acute treatment of children and adolescents with schizophrenia-spectrum disorders. (JAACAP)
- Maternal history of autoimmune disease has been linked to development of ADHD in offspring. (JAACAP)

The American Journal of Psychiatry

Volume 174, Issue 3

Internet Gaming Disorder: Investigating the Clinical Relevance of a New Phenomenon

Przybylski, et al.

Authors conducted four survey studies (N=18,932) with large international cohorts employed an open-science methodology. Among those who played games, more than 2 out of 3 did not report any symptoms of Internet gaming disorder, and findings showed that a very small proportion of the general population (between 0.3% and 1.0%) might qualify for a potential acute diagnosis of Internet gaming disorder. While internet gaming disorder did predict gaming engagement, no significant behavioral or clinical impact on individuals was reported. Study did not find evidence supporting a clear link to clinical outcomes.

Switch Rates During Acute Treatment for Bipolar II Depression with Lithium, Sertraline, or the Two Combined: A Randomized Double-Blind Comparison

Altshuler, et al.

This 16 week, double-blind, multisite comparison study randomly assigned 142 participants with bipolar II depression to receive lithium monotherapy, sertraline monotherapy or combination treatment of lithium and sertraline. The primary outcome measured was medication-induced mood switch risk, and secondary outcomes included treatment response and side effects. The results of the study demonstrated that 14% (N=20) of the study participants experienced a switch (hypomania, N=17; severe hypomania, N=3), but the switch rates did not differ among the three treatment groups even after controlling for dropout rates. None of the participants who experienced a mood switch had a manic switch or required hospitalization. Treatment response rates were also similar between all three groups. However, the lithium/sertraline combination group had a significantly higher overall dropout rate than the monotherapy groups and did not show any treatment acceleration advantage.

No Association of Lower Hippocampal Volume With Alzheimer's Disease Pathology in Late-Life Depression

De Winter, et al.

This prospective study sought to examine associations between decreased hippocampal volume in late-life depression and Alzheimer's disease pathology. Structural MRI, [18F]flutemetamol amyloid PET imaging, APOE genotyping, and neuropsychological assessment data from 48 depressed older adults and 52 healthy age- and gender-matched subjects were compared. A significant difference in mean normalized total hippocampal volume between the depressed adults and the healthy comparisons was identified. However, there were no group differences in cortical amyloid uptake or proportion of amyloid-positive subjects. There was no association between hippocampal volume and amyloid uptake in either the depressed group or the normal comparison group. These results counter the common belief that changes in hippocampal volume in late-life depression are due to prodromal Alzheimer's disease.

Haloperidol-Associated Uterine Dystonia

Ridout K. and Ridout S.

This case report highlights a previously overlooked side effect of haloperidol, uterine or fetal dystonia. In this case, an anti-psychotic naïve 27- year-old female at 25 weeks gestation was started on haloperidol 5mg as needed for anxiety or agitation and received 9 doses over 3 days. On day 4 of hospitalization, she developed cervical and limb dystonia, uterine contractions and increased fetal movements 2 hours after receiving haloperidol. These improved with benztropine and diphenhydramine.

JAMA Psychiatry

Volume 74, Issue 3

Impaired Glucose Homeostasis in First-Episode Schizophrenia: A Systematic Review and Meta-analysis

Pillinger, et al.

A meta-analysis of 14 case-control studies comprising 1345 participants sought to determine whether individuals with schizophrenia have an inherent risk for glucose dysregulation in the absence of the effects of chronic illness and long-term treatment. Antipsychotic-naïve individuals with first episode schizophrenia were compared to healthy individuals. Fasting plasma glucose levels, plasma glucose levels after an oral glucose tolerance test, fasting plasma insulin levels, and insulin resistance were all significantly elevated in patients when compared to controls. Only HBA1c levels were not altered in individuals with new-onset schizophrenia relative to controls. This study suggests that glucose homeostasis is altered from illness-onset in schizophrenia, not only with chronic illness and treatment effects.

Association of DSM-IV Posttraumatic Stress Disorder with Traumatic Experience Type and History in the World Health Organization World Mental Health Surveys

Liu, et al.

The World Health Organization analyzed surveys, which assessed 29 traumatic experience (TE) types (lifetime exposure, age at first exposure) with DSM-IV PTSD per the Composite International Diagnostic Interview. Among 34,767 respondents from 20 different countries, lifetime TE exposure was 70.3% with a 4.5 mean number of exposures. Weighted prevalence of PTSD associated with random TEs was 4.0%. Odds ratios of PTSD were elevated for TEs involving sexual violence and witnessing atrocities. Prior exposure to some traumatic experiences was associated with increased vulnerability (e.g., physical assault) or resilience (participation in sectarian violence).

Risk of Psychiatric Disorders Among Individuals With the 22q11.2 Deletion or Duplication: A Danish Nationwide, Register-Based Study

Hoeffding, et al.

This Danish-population based study of 3.7 million individuals sought to identify indicators of deletions or duplications at the 22q11.2 locus and estimate the incidence rate ratios and absolute risk for psychiatric disorders in affected individuals. The mean age at diagnosis of any psychiatric disorder was 12.5 years for those with deletions and 6.1 years for duplication carriers. Only a parental diagnosis of schizophrenia was associated with a deletion, but parental psychiatric disorders other than schizophrenia were associated with a duplication. For any psychiatric disorder, there was an increased risk for deletions and duplications. There was also a highly increased risk of intellectual disability for the deletion and duplication, but only the deletion showed an increased risk for pervasive developmental disorders and childhood autism.

Association Between Antipsychotic Agents and Risk of Acute Respiratory Failure in Patients with Chronic Obstructive Pulmonary Disease

Wang, et al.

A population-based case crossover-study used the Taiwan National Health Insurance Research Database to determine whether the use of antipsychotics is associated with an increased risk of acute respiratory failure (ARF) in patients with chronic obstructive pulmonary disease (COPD). In 5032 patients with newly diagnosed ARF identified from 61 620 patients with COPD, use of any antipsychotic was compared during days 1- 14 and days 75 to 88 preceding the ARF event. Of all patients with ARF, 11.7% filled at least one antipsychotic prescription during the 1-14 days compared to 8.8% during the control period, which corresponded to a 1.66 fold increased risk of ARF regardless of antipsychotic class or administration route. There was a dose-dependent risk of ARF with antipsychotics, which increased from 1.52 fold risk for a low daily dose to a 3.74 fold risk for a high dose.

Effect of Disorder-Specific vs Nonspecific Psychotherapy for Chronic Depression: A Randomized Clinical Trial

Schramm, et al.

In this randomized clinical trial of 268 adults with early-onset chronic depression, patients not taking antidepressant medication who were treated with the Cognitive Behavioral Analysis System of Psychotherapy (CBASP) reported significantly less severe depressive symptoms after 20 weeks than those who received nonspecific psychotherapy. This was evidenced by a 13.15 point decrease (from 27.15 to 14.00) on the 24-item Hamilton Rating Scale for Depression (HRSD-24) after 48 weeks of CBASP.

Association of Delirium With Cognitive Decline in Late Life: A Neuropathologic Study of 3 Population-Based Cohort Studies

Davis, et al.

This study aimed to examine whether the accelerated cognitive decline observed after delirium is independent of the pathologic processes of classic dementia in a cohort of 987 autopsied brains from 3 population-based cohort studies. Harmonized data from three unselected, population based cohort studies were analyzed, including repeated mental status assessments, detailed dementia evaluation, and neuropathologic autopsy findings. Interactions between pathologic burden and cognitive trajectory for the 6 years prior to death as estimated by MMSE scores were examined. Results showed that delirium and the pathologic processes of dementia were both independently associated with cognitive decline but that the combination of delirium and the pathologic processes of dementia interacted to give the fastest trajectory of cognitive decline.

The Journal of Clinical Psychiatry

Volume 4, Issue 2

Recovery from Anorexia Nervosa and Bulimia Nervosa at 22-Year Follow-Up

Eddy, et al.

Females with DSM-III-R/DSM IV anorexia nervosa or bulimia nervosa were assessed at 9 and 20 to 25 years of follow-up via structured clinical interview (Longitudinal Interval Follow-Up Evaluation of Eating Disorder [LIFE-EAT-II]). At 22-year follow-up, 62.8% of patients with anorexia nervosa and 68.2% of those with bulimia nervosa had recovered, compared with 31.4% with anorexia nervosa and 68.2% with bulimia nervosa at 9 years. Early recovery was associated with increased likelihood of long-term recovery in anorexia nervosa but not in bulimia nervosa. The authors suggest that findings argue against implementation of palliative care for most individuals with eating disorders.

High Rates of Psychiatric Comorbidity in Narcolepsy: Findings From the Burden of Narcolepsy Disease (BOND) Study of 9,312 Patients in the United States

Ruoff, et al.

This study found that narcolepsy is associated with a significant comorbid psychiatric illness burden and higher psychiatric medication use compared with the non-narcolepsy population. Specifically, there was a higher incidence of mood disorders (37.9% vs 13.8%), depressive disorders (35.8% vs 13.0%) and anxiety disorders (25.1% vs 11.9%) in the narcolepsy population relative to controls. In addition, there was significantly higher use of psychiatric medication in the narcolepsy group, including SSRIs, benzodiazepines, hypnotics, SNRIs and tricyclic antidepressants.

A Meta-Analysis of D-Cycloserine in Exposure-Based Treatment: Moderators of Treatment Efficacy, Response, and Diagnostic Remission

McGuire, et al.

This meta-analysis examined the efficacy of D-cycloserine-augmented exposure treatment in 20 randomized controlled trials (957 participants) on anxiety disorders, obsessive-compulsive disorder

(OCD), and posttraumatic stress disorder (PTSD). Specific treatment moderators (eg, comorbidity, medication status, gender, publication year) were found across conditions for both acute treatment and initial follow-up assessments. It was concluded that D-Cycloserine did not universally enhance treatment outcomes but did show promise for anxiety disorders. Future trials are needed to account for the identified moderators and as well as the mechanisms of D-Cycloserine to tailor treatment protocols and maximize its benefit.

High-Dose Citalopram and Escitalopram and the Risk of Out-of-Hospital Death

Ray, et al.

This study compared the risk of potential arrhythmia-related deaths in patients receiving high-dose citalopram (>40 mg) and escitalopram (>20 mg) compared to that for equivalent doses of fluoxetine, paroxetine, and sertraline. Data was analyzed from the Tennessee Medicaid Retrospective Cohort Study of 54,220 people from the ages of 30-74 (mean age 47 and 76% female) without cancer or other life threatening illness who were prescribed serotonin reuptake inhibitors (SSRIs) from 1998 to 2011. The respective hazard ratios (HRs) for citalopram versus escitalopram, fluoxetine, paroxetine, and sertraline were 0.84, 1.24, 0.75, and 1.53. The risk of sudden unexpected death, sudden cardiac death, or total mortality for high-dose citalopram and escitalopram did not differ significantly from that for comparable doses of fluoxetine, paroxetine, and sertraline.

The Lancet Psychiatry

Volume 4, Issue 3

Trajectories of relapse in randomized, placebo-controlled trials of treatment discontinuation in major depressive disorder: an individual patient-level data meta-analysis

Gueorguieva, et al.

This study analyzed patient data from four double-blind discontinuation clinical trials of duloxetine or fluoxetine versus placebo in major depression from before 2012. The study aimed to identify distinct trajectories of depression severity, assess whether similar or different trajectory classes exist for patients who continued or discontinued active treatment, and test whether clinical predictors of trajectory class membership exist using pooled data from clinical trials. Similar relapse trajectories were found for both active medication and on placebo, suggesting that there is no specific relapse signature associated with antidepressant discontinuation. Active treatment significantly lowered the odds of membership in the relapse trajectory (odds ratio 0.47), whereas female sex (1.56), shorter length of time with clinical response by 1 week (1.10), and higher clinical Global Impression score at baseline (1.28) increased the odds. Overall, the protective effect of antidepressant medication relative to placebo on the risk of being classified as a relapse was about 13% (33% vs 46%).

Lurasidone versus treatment as usual for cognitive impairment in euthymic patients with bipolar I disorder: a randomized, open-label, pilot study

Yatham, et al.

This randomized, open-label, pilot study aimed to examine the efficacy of lurasidone adjunctive therapy compared with treatment as usual (TAU) in improving cognition. The researchers recruited patients aged 19-65 years with euthymic bipolar I disorder from the Mood Disorder Centre in UBC Hospital (Vancouver, Canada). Between July 2, 2014 and Oct 19, 2015, 34 patients were randomly allocated to lurasidone adjunctive therapy (17 patients) or TAU (17 patients). Lurasidone adjunctive therapy was more effective than TAU in improving the primary efficacy measure of ISBD-BANC global cognition score (mean difference 2.92; $p=0.032$). The between-group effect size (0.82) on baseline versus study-end difference scores in the ISBD global cognition score was of moderate to large magnitude. The magnitude of benefit with lurasidone adjunctive therapy in improving global cognition (effect size 0.46) was greater compared with the improvement observed in the TAU group (0.04).

Reduction or discontinuation of antipsychotics for challenging behavior in adults with intellectual disability: a systematic review

Sheehan, et al.

This study reviewed the available evidence on the use of the antipsychotics to manage challenging behavior in adults with intellectual disability, which is widespread but controversial. The researchers found that antipsychotics can be reduced or discontinued in a substantial proportion of adults who use them for challenging behavior, although not always without adverse effects. There is a group which displays behavioral deterioration on antipsychotic reduction that prevents discontinuation; predictors of poor response could not be reliably identified. In view of the relatively scarce data and methodological limitations of the available studies, the researchers could not draw firm conclusions to inform a population level approach to this issue. They recommend that antipsychotic medication used for behavior should be reviewed regularly and an individualized approach should be taken to treatment.

Financial incentives for improving adherence to maintenance treatment in patients with psychotic disorders (Money for Medication): a multicentre, open-label, randomised controlled trial

Noordraven, et al.

This multicenter, randomized controlled trial study from 2010 to 2014 in the Netherlands assessed the effectiveness of giving financial incentives to improve adherence in patients taking antipsychotic depot medications irrespective of their previous compliance. Patients were between the age of 18-65, had been diagnosed with schizophrenia or another psychotic disorder, had been prescribed antipsychotic depot medication or had an indication to start using depot medication, and were participating in outpatient treatment. Patients who were randomly assigned to the financial incentive group, 169 in total, received 30 Euros per month if fully compliant. The primary outcome was the Medication Possession Ratio (MPR), defined as the number of depots of antipsychotic medication received divided by the total number of depots of antipsychotic medication prescribed during the 12 month intervention period. At the end of the

12 month period the mean MPR was higher in financial incentive group (94.3%) than in the control group (80.3%) indicated that financial incentives could be an effective way of improving adherence to antipsychotic depot medication.

Journal of the American Academy of Child and Adolescent Psychiatry

Volume 56, Issue 3

Acute Antipsychotic Treatment of Children and Adolescents with Schizophrenia-Spectrum Disorders: A Systematic Review and Network Meta-Analysis

Pagsberg, et al.

This meta-analysis combined indirect and direct trial data to determine the comparative efficacy and safety of antipsychotics for youth with early-onset schizophrenia. The authors selected randomized controlled trials of youth with schizophrenia spectrum disorders to a non-clozapine antipsychotic versus placebo or another antipsychotic. Major efficacy outcomes included the Positive and Negative Syndrome Scale (PANSS) total and positive symptoms. Major safety outcomes were weight, plasma triglyceride levels, extrapyramidal symptoms, akathisia, and all-cause discontinuation. Twelve 6-12 week trials involving antipsychotics (aripiprazole, asenapine, paliperidone, risperidone, quetiapine, olanzapine, molindone, and ziprasidone) were analyzed. Among antipsychotics, PANNS total symptom change was comparable with exception for ziprasidone. All antipsychotics, with exception of ziprasidone and asenapine were superior to placebo. Weight gain was primarily associated with olanzapine. Extrapyramidal symptoms were associated with molindone, and prolactin increase was associated with risperidone, paliperidone, and olanzapine.

Mental Health in Internationally Adopted Adolescents: A Meta-Analysis

Askeland, et al.

This meta-analysis aimed to assess whether mental health problems differ between internationally adopted adolescents and their non-adopted peers. Eleven studies investigating 17, 919 adoptees and 1, 090, 289 non-adopted peers were included in the meta-analysis. Internationally adopted adolescents reported more mental health problems across domains than their peers and reported more externalizing difficulties. The difference in mental health problems between the two groups was larger when using parent report compared with self-report. No significant difference was found for the subgroup analysis investigating sex and age at adoption.

Associations Between Autoimmune Diseases and Attention-Deficit/Hyperactivity Disorder: A Nationwide Study

Nielsen, et al.

This study investigated the association between a personal history and a family history of autoimmune disease and the risk of developing attention-deficit/hyperactivity disorder (ADHD). The population

studied consisted of 983, 680 individuals born in Denmark from 1990 to 2007. Information on autoimmune diseases and ADHD was obtained through national registries. Autoimmune disease in the individual was associated with an increased risk of ADHD with an incidence rate ratio of 1.24. Maternal autoimmune disease was associated with ADHD in the offspring whereas a paternal history of autoimmune disease was not significantly associated. Specific autoimmune diseases associated with ADHD included a family history of thyrotoxicosis, type I diabetes, autoimmune hepatitis, psoriasis, and ankylosing spondylitis.

Predictors and Outcomes of Childhood Primary Enuresis

Kessel, et al.

Authors of this study examined the prevalence, predictors, prognostic factors, and outcomes of primary enuresis in a large multi-method, multi-informant prospective study with a community-based sample of children followed from age 3 years to age 9 years. Males were more than twice as likely as females to have a lifetime diagnosis of enuresis. Significant predictors of developing primary enuresis by age 9 included childhood anxiety and low positive affectivity, maternal history of anxiety, and low authoritative parenting. Poorer global functioning and more depressive and anxiety symptoms predicted a greater likelihood of persistence through age 9. By age 9 years, three-fourths of children who had received a diagnosis of primary enuresis were in remission and continent. Children who had remitted exhibited a higher rate of ADHD and greater ADHD and depressive symptoms at age 9 compared to children with no lifetime history of enuresis.

Journal of the American Psychoanalytic Association

Vol 65, Issue 1

Moving from within the Maternal: The Choreography of Analytic Eroticism

Elise D.

Using Kristeva's ideas about maternal eroticism, Elise explores the parallel engagements between patient and analyst. She goes on to suggest that the analyst's activity is similar to choreography in dance and expands on notions of erotic transference/countertransference.